

# Bioinformatics

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Several methods have been proposed to perform power and sample size calculations for a microarray study that will use FDR-type measures of significance in the final analysis. [37, 38] However, most of these methods are designed only for two-group designs, such as studies that compare tumor expression to normal expression. Pounds and Cheng (2005) [39] describe a general method to perform power and sample-size calculations for studies that will use the FDR to determine significance in the final analysis. For  $i = 1, \dots, m$ , their method assumes that cumulative distribution function of  $P_i$ ,  $G_i(\cdot; \delta_i, n)$  can be computed given the sample size  $n$  and an effect size  $i$ . Their method uses the *average power* (AP) as a measure of statistical power. The average power is defined as the arithmetic average of the powers of the tests with a true alternative. Under model (1), the average power is simply  $AP(\alpha) := H_m(\alpha; \Delta, n)$ .

The sample size determination procedure uses the *anticipated false discovery rate* (aFDR),  $aFDR(\alpha, \Delta, n) := \hat{E}(\hat{\pi}_0; \Delta, n)\alpha / F_m(\alpha; \Delta, n)$  to perform its calculations. The ensemble P value cdf  $F_m(\cdot; \Delta, n)$  is either postulated or estimated from preliminary data. The method is designed to determine the sample size necessary to achieve an average power of  $\gamma$  while keeping the aFDR below  $\tau$ . The values of  $\gamma$  and  $\tau$  must be chosen by the user. The method proceeds iteratively. With an initial sample size  $n_0$  and a specified value or estimate for  $\Delta$ , the procedure first finds  $\alpha^*$  such that  $AP(\alpha^*) = \gamma$ . Then, it computes  $aFDR(\alpha^*)$ . If  $aFDR(\alpha^*) \leq \tau$ , then the procedure reports that  $n_0$  is an adequate sample size to achieve average power  $\gamma$  while keeping the aFDR below  $\tau$ . Otherwise, it increments  $n$  and repeats the calculations. The process is iterated until a maximum sample size is reached or the conditions for the aFDR and AP are satisfied. Pounds and Cheng (2005) [39] also describe a method to estimate necessary parameters from pilot data. They observed that the parameter-estimation and sample-size calculation method performed well in traditional simulation studies and in resampling-based simulation studies performed using real data.